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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/515,283 02/29/00 AGHASSI

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EXAMINER

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ART UNIT	PAPER NUMBER

1641
DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/515,283

Applicant(s)

AGHASSI et al.

Examiner
James L. Grun, Ph.D.

Group Art Unit
1641



☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-16 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-16 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

During a telephone conversation with Mr. Daniel D. Chapman on 16 October 2000 a restriction requirement between the inventions of claim 1 (Group I), claims 2-5 (Group II) , and
5 claims 6-16 (Group III) was proposed and a provisional election was made to prosecute the invention of Group III, claims 6-16. However, upon reconsideration, the examination of all claims in the application was not found burdensome by the Examiner and the inventions have been re-joined herein for examination on the merits.

The disclosure is objected to because of the following informalities: the specification contains
10 grammatical and spelling errors too numerous to mention specifically and should be carefully revised. Examples of such errors are: --No.-- should be at line 9 of page 2; --surfactants-- should be at line 19 of page 4; --58°C-- should be at line 2 of page 12; etc. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

15 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with that as instantly claimed.

Applicant teaches and exemplifies deparaffinizing antigen retrieval solutions which are heated for use. As taught by Shi et al (J. Histochem. Cytochem. 43: 193-201, 1995), heat plays a critical role in the immunohistochemical enhancement of such antigen retrieval solutions. Moreover, Yörükoğlu et al (Appl. Immunohistochem. 5: 71, 1997) teach, what is notoriously old and well known in the art, that heating melts paraffin. It is unknown and entirely unpredictable, absent any description and guidance from Applicant, whether the components of the solution or the exemplified, and apparently essential, heating of the solution performs the functions of embedding medium removal and/or immunohistochemical staining/antigenicity enhancement. Absent further description and guidance from Applicant, one would not be assured of any predictable ability to formulate and

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provide a composition with such components for use in the methods with the properties as instantly claimed.

Insufficient guidance is provided with regard to which specific reagents can be combined into a solution in claims 1 and 6-16 with predictable function in the invention. For example, metal salts, as suggested for use, are not generally conducive to effective surfactant activity. Absent further description and guidance from Applicant, random unguided unpredictable experimentation would seem to be required to determine compositions which function in the invention and those that do not. The providing of a desired goal for properties of a composition, and a listing of possible alternatives from which to perhaps formulate such a composition, is not seen as providing an enabling disclosure for those specific compositions which predictably function in the invention. Such experimentation, essentially allowing another to perhaps identify what Applicant claims as the invention, is undue.

Further, it would seem unknown and entirely unclear and unpredictable that the suggested compositions function with anything other than aldehyde-fixed paraffin-embedded tissues. In this regard, Shi et al (J. Histochem. Cytochem. 39: 741-748, 1991) teach that the antigen retrieval method does not function with alcohol-fixed tissue samples (e.g. page 746). Any ability of the instantly suggested compositions to remove and enhance immunohistochemical staining of celloidin-embedded or acrylamide-embedded tissue samples would also appear unknown and unpredictable.

Moreover, in claims 6-16, absent any guidance from Applicant, one would not know what other stains are amenable to the preparation method other than immunohistochemical staining because it is not clear what other unmasking or activating of tissue would be required.

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For the reasons set forth above, the specification does not provide adequate guidance and does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

5 Claims 3 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for addition of a 25% volume of SIMPLE GREEN® surfactant (see e.g. page 11), does not reasonably provide enablement generally for a 25% volume of surfactants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As the concentration of surfactants can be adjusted in any stock solution, one would not know what
10 surfactant concentrations were encompassed or not encompassed by the claims, other than a 25% volume of SIMPLE GREEN® surfactant, and would not be assured of the ability to use another composition of indeterminate surfactant concentration in the invention as disclosed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

15 The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 1, "adapted to" is not clear as to what is encompassed.

In claims 2 and 4, "the antigenicity" and "the pH" lack antecedent basis. At line 3, "A buffered" should be --a buffered--. At line 3, it is believed that --moles-- was intended. At line 3, "dehydrate" should be --dihydrate--. It is not clear what is encompassed by a "sufficient reagent".

5 Claims 2 and 4 contain the trademark/trade name SIMPLE GREEN®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or
10 trademark is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an aqueous surfactant solution containing, by weight, about 5.8% ethylene glycol monobutyl ether, about 3.75% nonylphenol ethoxylate, and about 1.5% tetrapotassium pyrophosphate (see e.g. U.S. Patent No.
15 5,856,289) and, accordingly, the identification/description is indefinite.

In claims 3 and 5, "the antigenicity" and "the pH" lack antecedent basis.

In claims 4 and 5, it is not clear what functions or components are encompassed by or in an "appropriate" buffer. The Examiner suggests the insertion of the intended use recitations of the composition claims into the preambles of the method claims and insertion at line 3 of the claims, after
20 composition, --of Claim...--.

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In claims 6-16, "the receipt" lacks antecedent basis. It is not clear what is encompassed by a "single liquid composition" and if the components recited in the dependent claims are in addition to the components in the composition already capable of the recited functions.

In claim 8, "when" is not clear.

5 In claim 9, "the" concentration range lacks antecedent basis and it is not clear on what basis the percentage is determined.

In claim 10, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable. In the claim, "the detergent" lacks antecedent basis.

10 In claims 13-14, "the" pH lacks antecedent basis.

In claim 15, it is believed that --biodegradable-- was intended and it is not clear what is encompassed within the metes and bounds of the claim.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

15 A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Thorne (US 5,552,294), if necessary in light of Cattoretti et al (J. Pathol. 171: 83-98, 1993) and the instant disclosure.

Thorne teaches an aqueous composition comprising a surfactant, urea, a Tris buffer, and polymyxin B (see e.g.: columns 6-8; and, column 9, "Reagents" table) which, absent evidence to the contrary, anticipates the instant composition because the composition of the reference has all of the components as instantly claimed which are inherently capable of performing the functions as disclosed and recited. In one interpretation, in view of the teachings of the reference or in light of the teachings of Cattoretti et al, the urea of the prior art composition is considered herein as one component which performs the immunological staining enhancement function of the "activating agent". In another interpretation, the buffer performs the "activating agent" function, in light of the instant disclosure. Recitations of intended use, i.e. "adapted to", have been accorded weight only to the extent that such recitations limit the composition. Such recitations do not distinguish the prior art composition from that as instantly claimed.

Claim 1 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Shi et al (WO 94/04906).

Shi et al teach solutions comprising solvents, which may solubilize an embedding medium, enhancing additives, and aldehyde releasing reagents (i.e. "activating agent") (see e.g. pages 8-10).

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Claims 3 and 5 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Yörükoğlu et al (Appl. Immunohistochem. 5: 71, 1997).

Yörükoğlu et al (Appl. Immunohistochem. 5: 71, 1997) teach deparaffinization, hydration, and antigen retrieval for immunohistochemistry in a simultaneous step, with one change of the tissue section on the adhesive-coated slide from a first to a second container of simultaneously heated antigen retrieval solutions to rinse off and minimize melted paraffin smearing. A microwave oven is used as the heating means. It is noted by the Examiner that there is no lower limit for the recited components of the composition and, as such, 0% levels are encompassed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

(c) Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

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Claims 1-16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Hazelbag et al (J. Histochem. Cytochem. 43: 429-437, 1995), Shi et al (J. Histochem. Cytochem. 43: 193-201, 1995), and Yörükoğlu et al (Appl. Immunohistochem. 5: 71, 1997).

Shi et al (J. Histochem. Cytochem. 43: 193-201, 1995) teach antigen retrieval immunohistochemistry methods and compositions. A variety of buffer compositions are taught as the antigen retrieval solution. The reference teaches the critical effects of temperature and pH on the process and that the composition of the buffer is not as important a factor as the pH of the solution (see e.g. pages 197 and 199). A microwave oven is used as the heating means. However, the reference teaches deparaffinization prior to antigen retrieval.

Hazelbag et al (J. Histochem. Cytochem. 43: 429-437, 1995) teach a detergent solution, comprising ionic and non-ionic surfactants, as a preferred antigen retrieval solution for immunohistochemistry. A microwave oven is used as the heating means. However, the reference teaches deparaffinization prior to antigen retrieval.

The teachings of Yörükoğlu et al (Appl. Immunohistochem. 5: 71, 1997) are as set forth previously in this Office action.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have incorporated a buffer, as taught by Shi et al, in the detergent antigen retrieval solution of Hazelbag et al for use in any of the antigen retrieval method variations taught in any of Hazelbag et al, Shi et al, or Yörükoğlu et al because of the important effect of pH on the function of an antigen retrieval solution taught by Shi et al. One would have had obvious motivation to have

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formulated and used an antigen retrieval solution comprising a detergent in any of the antigen retrieval method variations taught by the references in view of the improved function of such a solution for antigen retrieval taught in Hazelbag et al. As Hazelbag et al teach a detergent solution comprised of a surfactant mixture, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted any functionally equivalent surfactant in the composition of Hazelbag et al, as modified by Shi et al, with a reasonable expectation of success that the surfactant would perform the desired function in the composition and method. It would have been further obvious to have performed the antigen retrieval method using any antigen retrieval solution, such as those taught by the combination of Hazelbag et al with Shi et al, with the method modification of Yörükoğlu et al for the ease and time savings taught therein. It would have been further obvious to have incorporated a dye in the composition, as is notoriously old and well known in the art, for such purposes as identification or visual pH determination of the solution.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hazelbag et al, Shi et al, and Yörükoğlu et al as applied to claims 1-16 above, and, if necessary, further in view of either of Norton et al (J. Pathol. 173: 371-9, 1994) or Miller et al (Applied Immunohistochem. 3: 190-3, 1995).

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The teachings of the Hazelbag et al, Shi et al, and Yörükoğlu et al are as set forth above and differ from the invention as instantly disclosed in not teaching heating at the elevated pressure and temperature achievable in a pressure cooker.

Norton et al or Miller et al teach a pressure cooker as an alternative to a microwave oven as the heating means for antigen retrieval.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted a pressure cooker for the microwave oven as the heating means in the antigen retrieval method modification of Hazelbag et al, Shi et al, and Yörükoğlu et al in view of the express teaching of the substitution by either of Norton et al or Miller et al for the benefits taught therein.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claim 3 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Ding et al. Ding et al teach a buffered surfactant composition. The buffer system may be any common buffer such as citrate.

Claim 3 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Prieto (U.S. SIR H1478). Prieto teaches a surfactant composition which may contain a builder, which may comprise a citrate salt, for purposes such as buffering (see e.g.: columns 5-6; Table I).

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It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have provided stock solutions in varying concentrations to be mixed in varying proportions, such as using a 4X concentrated surfactant stock, in formulating the compositions of Ding et al or Prieto because such variation in mixing stock solutions to provide a final working reagent is routine in the art motivated by design or convenience. Note also that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Note that the intended use of a composition is accorded patentable weight only to the extent that it limits the actual components therein. In the instant case the intended use does not serve to distinguish the instant composition from that disclosed in the references. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

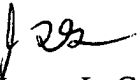
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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to James L. Grun, Ph.D., Technology Center 1600, Group 1640, Art Unit 1641, whose telephone number is (703) 308-3980. The Examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

- 5 If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Long Le, SPE, can be contacted at (703) 305-3399. The fax phone numbers for official communications to Group 1640 are (703) 305-3014 or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

10


James L. Grun, Ph.D.
October 20, 2000



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PRIMARY EXAMINER
GROUP ~~1800~~-1641